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Increased thyroid hormones and autoantibodies levels associated with quasi-moyamoya disease

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Abberviations: MMD: Moyamoya disease; T3: Triiodothyronine; T4: thyroxine; TSH: Thyroid-stimulating hormone; TGAb: Antithyroglobulin antibody; TPOAb: Antithyroperoxidase antibody; TRAb: Thyrotropin receptor antibody.

Abstract

Objectives: The purpose of this study was to investigate whether elevated thyroid autoantibodies associated with quasi-Moyamoya Disease (MMD).

Methods: We retrospectively investigated angiographically defined patients with quasi-MMD patients. We compared clinical features, serum thyroid autoantibody values and T cell levels between quasi-MMD patients and control subjects.

Results: A total of 103 patients with MMD and an equal number of healthy control subjects (n=103) were included. The prevalence of elevated thyroid autoantibodies (P=0.008) were significantly higher in patients with MMD than in control subjects. The increased thyroid hormone (OR, 11.03; 95% CI, 1.22 to 96.13; P=0.034) and

Increased thyroid autoantibodies (OR, 6.38; 95% CI, 1.12 to 46.52; P=0.040) were significantly associated with increased risks of quasi-MMD, respectively. The antithyroid therapy can significantly attenuate disease progression than without special treatment in quasi-MMD patients with thyroid disease (P=0.041).

Conclusions: Increased thyroid hormone and thyroid autoantibodies levels in serum were significantly in association with quasi-MMD. Antithyroid therapy may significantly attenuate or slow disease progression in quasi-MMD with thyroid disease patients. The results suggested that both abnormal thyroid hormones and elevated thyroid autoantibodies played important roles in MMD development, which might help to better manage and further study underlying pathogenesis mechanisms of quasi-MMD.

Background

The increased thyroid hormones and elevated thyroid autoantibodies were found frequently in quasi-Moyamoya Disease (MMD) patients, indicating increased thyroid function and elevated thyroid autoantibodies were associated with patients with MMD [1-4]. Whether increased thyroid hormones and elevated thyroid autoantibodies were associated with quasi-MMD patients remains to be explored. Using case-control and retrospective cohort study, we explored and compared clinical features, serum thyroid hormones and autoantibodies levels, and analyzed disease progression between quasi-MMD patients and control subjects, to elucidate whether abnormal increased thyroid hormones and elevated thyroid autoantibodies associated with quasi-MMD.

Methods

We retrospectively included with quasi-MMD (confirmed by digital subtraction angiography) patients admitted to our hospital, from August 2016 to June 2023. We included MMD patients

with Graves disease, thyroid goiter, Hashimoto thyroidistis and apparent euthyroid state. Sex and age-matched healthy controls (confirmed by physical examination) were recruited in this study. All study subjects were residents of central China.

Features, including smoking and hypertension history, hyperlipidemia, abnormal homocysteme and family history of cerebrovascular disease.

Serum triiodothyronine (T3), free T3, thyroxine (T4), free T4, Thyroid-Stimulating Hormone (TSH), antithyroglobulin antibody (TGAb), antithyroperoxidase antibody (TPOAb), and Thyrotropin Receptor Antibody (TRAb) were examined by employing electrochemical luminescence. When serum TGAb>115 IU/L, or TPOAb>34 IU/L, or TRAb>3 IU/L was identified as elevated thyroid autoantibodies according to the manufacturer' reference values.

Data were analyzed by employing IBM SPSS 26.0 (Chicago, IL, USA). Continuous variables were analyzed by independent-samples t test, whereas categorical variables were analyzed by Pearson c2 test. Forward stepwise conditional logistic regression analysis was conducted to investigate the correlation of abnormal thyroid hormones and elevated thyroid autoantibodies with quasi-MMD. Any variable from the univariate analysis at P<0.15 were considered to be included.

The effects of antithyroid therapy on disease progression of patients with MMD were assessed by using retrospective cohort design during follow-up period.

Results

Clinical and laboratory characteristics are presented in Table 1. In the study, 65 of 103(63.1%) patients with quai-MMD were female, and the average age was 41.1±13.8 years. And 33 of 103(32.0%) patients was association with increased thyroid hormones and thyroid autoantibodies levels, at average age of 38.1±12.6 years, and 30(90.9%) was female. Multivariate analysis indicated that the female with thyroid cerebrovascular disease, smoke, hypertension, diabetes, hyperlipidemia and homocysteme were not association with MMD when compared with control subjects.

Thyroid hormones examinations displayed that average values of serum T3, free T3, T4, free T4 and TSH were significantly increased in quasi-MMD patients comparison with control subjects (P<0.05 for all). Thyroid dysfunction were significantly higher in quasi-MMD patients than in control subjects (31.6% versus 1.9%, P=0.000).

Increased thyroid autoantibodies were detected in 35 of 103 patients with MMD. The increased thyroid autoantibodies were significantly higher in quasi-MMD patients than in healthy control subjects (35.3% versus 2.9%, P=0.000). TGAb, TPOAb and TRAb were significantly higher in quasi-MMD than in healthy control subjects (24.3% versus 1.9%, P=0.000; 33.0% versus 2.9%, P=0.000; 14.6% versus 0%, P=0.006, respectively).

Forward stepwise conditional logistic regression analysis further assessed the correlation of increased thyroid hormones and autoantibodies with quasi-MMD. After adjusting the covariates, including age, sex, smoking, hypertension, diabetes, hyperlipidemia, homocysteme, family history of cerebrovas-

Table 1: Baseline clinical and laboratory features of onset in quasi-MMD patients and control subjects.

	MMD (103)	Conrols (103)	P-Value
Age, Years	38.5±12.1	39.0±10.8	
Female	63.1	62.1	
Current smoker	14.6	15.5	0.802‡
Hypertension	24.3	19.4	0.731‡
Diabetes	8.7	4.9	0.608‡
Hyperlipidemia	15.5	9.7	0.196‡
Homocysteme	15.5	6.8	0.148‡
Family history of cerebralvascular disease	17.5	14.6	0.786‡
sTHT			
TSH, mU/L [0.27-0.42]	1.58±1.46	2.12±1.36	0.077†
T3, nmol/L [1.30-3.10]	2.67±0.54	1.65±0.5	0.002†
Free T3, pmol/L [3.60-7.50]	5.89±2.36	4.46±1.28	0.003†
T4, nmol/L [62-164]	121.6±45.6	60.5±20.9	0.002†
Free T4, pmol/L [12.0-22.0]	22.31±10.58	14.25±2.69	0.035†
Thyroid function abnormalities			
Increased thyroid hormones	31.6	1.9	0.000‡
Subclinical hyperthyroidism	13.6	1.9	0.029‡
Overt hyperthyroidism	17.5	NA	0.000‡
Decreased thyroid function	2.9	1.9	1.000‡
Subclinical hypothyroidism	3.9	1.9	
Elevated thyroid autoantibodies	35.3	2.9	0.000‡
TGAb-positive	24.3	1.9	0.000‡
TPOAb-positive	33.0	2.9	0.000‡
TRAb-positive	14.6	NA	0.000‡

Numbers in brackets are reference ranges. Quasi-MMD indicates quasi-moyamoya disease; sTHT, serum thyroid hormones tests; TGAb, antithyroglobulin antibody; TPOAb, antithyroperoxidase antibody; TRAb, thyrotropin receptor antibody. Data presented as mean±SD or percentage (%). NA, not available. †Independent-samples t test. ‡ Pearson c^2 test.

Table 2: The summary of disease progressions in MMD with and without elevated thyroid autoantibodies.

	Quasi-MMD after antithyroid treatment	Quasi-MMD without antithyroid treatment	P-Value
No. of persons	76	27	
Follow-up (months)	44.2±17.6	42.2±12.1	0.896†
Age, years	38.0±8.2	36.2±16.2	0.712‡
Female	85.5	51.8	0.000‡
Disease progression	10.5(n=8)	29.6 (n=8)	0.019‡

Data presented as mean±SD or percentage (%). †Independent-samples t test. ‡ Pearson c^2 test.

cular, the increased thyroid hormone (OR, 11.03; 95% CI, 1.22 to 96.13; P=0.034) and increased thyroid autoantibodies (OR, 6.38; 95% CI, 1.12 to 46.52; P=0.040) were significantly associated with quasi-MMD, respectively.

During follow-up period (from 6 mo to 72 mo, mean 43.2±14.2 months), 8 of 76(10.5%) quasi-MMD patients who were treated with antithyroid therapy involved in disease progression. 8 of 27(29.6%) quasi-MMD patients without antithyroid therapy prevalence of disease progression was significantly lower in quasi-MMD patients with antithyroid therapy than in quasi-patients MMD without antithyroid treatment (10.5% versus 29.6%, p=0.043, 0R 1.003, 95% CI 0.970 to 12.186; Table 2).

Discussion

In the this respective study, we analyzed the clinical features, serum thyroid hormones and thyroid autoantibodies levels and assessed disease progression in quasi-MMD patients. We can get the following results: 1) The sex and age features of onset predominately affected the female, and female patients with quasi-MMD had a higher risk than male patients in association with thyroid disease; 2) Antithyroid treatment could attenuate disease progression in quasi-MMD with thyroid disease; 3) These clinical characteristics and laboratory values also demonstrated increased thyroid hormones and thyroid autoantibodies levels associated with quasi-MMD patients [4-7].

In the study, we found that about 31.6% of quasi-MMD patients displayed overt plus subclinical thyroid dysfunction and up to 35.3% of quasi-MMD patients displayed increased thyroid autoantibodies. Especially noteworthy, both increased thyroid hormones and thyroid autoantibodies were significantly associated with quasi-MMD after adjusting the covariates. There were several possible reasons for explanation [8-11]. First, thyrotoxicosis was known to result in changes in cerebral hemodynamics that may increase brain metabolism and oxygen consumption, which is harmful to the artery wall.

Secondly, there is an excess of thyroid hormone, which causes a long-term increase in sympathetic nervous system activity and may be involved in the formation of a narrowing or occlusion of brain arteries. Finally, increased thyroid autoantibodies simultaneously with Graves' disease and moyamoya-like vascular changes. Previous studies suggested the underlying common mechanism between these two entities is T-cell dysfunction, which involved in immunologic stimulation of thyroid gland thyroid autoimmune disease. All above might involve in cellular proliferation and vascular vascular remodeling of intracranial artery in quasi-MMD [12,13]. Therefore, both increased thyroid hormones and thyroid autoantibodies could be associated with quasi-MMD.

The association that increased thyroid hormones and thyroid autoantibodies with quasi-MMD development was further demonstrated when compared disease progression in quasi-MMD patients after antithyroid treatment. To our knowledge, previous studies rarely explored disease progression in quasi-MMD patients by treatment reducing the levels of thyroid hormones and thyroid autoantibodies. Chronic disease progression such as cerebrovascular stroke is feature of patients with quasi-MMD [14,15]. The quasi-MMD after thyroid treatment had significantly less disease progression than quasi-MMD patients without special treatment. The results suggested that normal thyroid hormones and autoantibodies might play protective effect on disease progression in quasi-MMD patients with thyroid disease. However, abnormal increased thyroid hormones and autoantibodies may induce arterial stenosis and occlusion in quasi-MMD [15,16]. It was thought that physiological thyroid hormones and autoantibodies levels which maintained normal cerebral hemodynamics and sympathetic nervous system activity could not be harmful to intracranial arterial walls. Therefore, the disease progression does not continue [3,17]. In addition, immune stimulation and inflammatory response in quasi-MMD patients may stop under physiological levels of thyroid autoantibodies [18-20].

Previous studies have shown that patients with Graves' disease and patients with elevated levels of anti-thyroid peroxidase antibodies have terminal carotid artery stenosis and occlusion, while patients with normal thyroid function or with no elevated levels of thyroid antibodies have mostly stenosis in the middle cerebral artery [20,21]. The lesion of the end of the internal carotid artery was associated with increased thyroid antibody level and enhanced thyroid function. The stenosis found at the end of the internal carotid artery and immune-mediated thyroid disease may share a common background [20-22]. The changes of cerebral vascular hemodynamics induced by thyrotoxicosis may be one of the causes of ischemic accidents [23,24]. Previous studies have shown that patients with Graves' disease and patients with elevated levels of anti-thyroid peroxidase antibodies have terminal carotid artery stenosis and occlusion, while patients with normal thyroid function or with no elevated levels of thyroid antibodies have mostly stenosis in the middle cerebral artery [20,21]. The lesion of the end of the internal carotid artery was associated with increased thyroid antibody level and enhanced thyroid function. The stenosis found at the end of the internal carotid artery and immune-mediated thyroid disease may share a common background [20-22]. The changes of cerebral vascular hemodynamics induced by thyrotoxicosis may be one of the causes of ischemic accidents [23-25]. The excessive thyroid hormone is harmful to the artery wall, and increased sympathetic nerve activity in thyrotoxicosis leads to intracranial artery stenosis [26,27]. Yoshimoto, et al suggested that thyroid autoantibodymay be an important factor in transient ischemic attacks, and association between thyroid autoantibody levels and Moyamoya disease susceptibility gene RNF213 p.R4810K variants [28].

Conclusion

In conclusion, both increased thyroid hormones and thyroid autoantibodies were significantly associated with quasi-MMD. Antithyroid treatment could significantly attenuate or slow disease progression in quasi-MMD with thyroid disease. Both increased thyroid hormones and elevated thyroid autoantibodies involved immune abnormalities also play underlying roles in quasi-MMD development, which was helpful for the management and research of this disease of quasi-MMD.

References

1. Santoro JD, Lee S, Wang AC, et al. Increased Autoimmunity in Individuals With Down Syndrome and Moyamoya Disease.Front Neurol. 2021 Sep 8;12:724969.
2. Lanterna LA, Galliani S, Zangari R, et al. Thyroid Autoantibodies and the Clinical Presentation of Moyamoya Disease: A Prospective Study. J Stroke Cerebrovasc Dis. 2018 May;27(5):1194-1199.
3. Lanterna LA, Galliani S, Brembilla C, et al.Association of moyamoya disease with thyroid autoantibodies and thyroid function. Eur J Neurol. 2017 Feb;24(2):e9.

4. Tanaka M, Sakaguchi M, Yagita Y, et al. Thyroid antibodies are associated with stenotic lesions in the terminal portion of the internal carotid artery. Eur J Neurol. 2014 Jun;21(6):867-73.

5. Kim SJ, Heo KG, Shin HY, et al. Association of thyroid autoantibodies with moyamoya-type cerebrovascular disease: a prospective study. Stroke. 2010.Jan;41(1):173-6.

6. Ahn JH, Jeon JP, Kim JE, et al. Association of Hyperthyroidism and Thyroid Autoantibodies with Moyamoya Disease and Its Stroke Event: A Population- based Case-control Study and Meta-analysis. Neurol Med Chir (Tokyo). 2018 Mar 15;58(3):116-123.

7. Gonzalez NR, Amin-Hanjani S, Bang OY, et al.Adult Moyamoya Disease and Syndrome: Current Perspectives and Future Directions: A Scientific Statement From the American Heart Association/American Stroke Association. Stroke. 2023 Aug 23. doi: 10.1161/STR.0000000000000443.

8. Vanderpump MPJ. The epidemiology of thyroid disease. British Medical Bulletin 2011;99:39-51.

9. Hiruma M, Watanabe N, Mitsumatsu T, et al. Clinical features of moyamoya disease with Graves' disease: a retrospective study of 394,422 patients with thyroid disease. 2023 Feb 28;70(2):141-148.

10. Suzuki S, Mitsuyama T, Horiba A, Fukushima S, Hashimoto N, Kawamata T. Moyamoya disease complicated by Graves' disease and type 2 diabetes mellitus: Report of two cases. Clin Neurol Neurosur 2011;113:325-329.

11. Squizzato A, Gerdes VE, Brandjes DP, Buller HR, Stam J. Thyroid diseases and cerebrovascular disease. Stroke 2005; 36:2302-2310.

12. Gill JH, Nam TK, Jung HK, et al. Acute cerebral infarction combined with a thyroid storm in a patient with both Moyamoya syndrome and Graves' disease. J Cerebrovasc Endovasc Neurosurg. 2022 Jun;24(2):160-165.

13. Ihara M, Yamamoto Y, Hattori Y, et al. Moyamoya disease: diagnosis and interventions. Lancet Neurol. 2022 Aug;21(8):747-758.

14. Inaba M, Henmi Y, Kumeda Y, et al. Ishimura E, Nishizawa Y. Increased stiffness in common carotid artery in hyperthyroid Graves disease patients. Biomed Pharmacother 2002;56:241-246.

15. Velo M, Grasso G, Fujimura M, et al. Moyamoya Vasculopathy: Cause, Clinical Manifestations, Neuroradiologic Features, and Surgical Management. World Neurosurg. 2022 Mar;159:409-425.

16. Czarkowski M, Hilgertner L, Powalowski T, Radomski D. The stiffness of the common carotid artery in patients with Graves' disease. Int Angio 2002;21:152-157.

17. Zhang X, Xiao W, Zhang Q, et al. Progression in Moyamoya Disease: Clinical Features, Neuroimaging Evaluation, and Treatment. Curr Neuropharmacol. 2022;20(2):292-308.

18. Paneggres PK, Morris JG, O'Neill PJ, Balleine R. Moyamoya-like disease with inflammation. Eur Neurol 1993;33:260-263.

19. Singh R, McLelland MD, De La Peña NM, et al. Research advances in the diagnosis and treatment of moyamoya disease: a bibliometric analysis. Neurosurg Rev. 2022 Jun;45(3):1977-1985.

20. Conklin JM, Fierstra JM, Crawley AP, et al. Impaired cerebrovascular reactivity with steal phenomenon is associated with increased diffusion in white matter of patients with Moyamoya disease. Stroke. 2010; 41: 1610-1616.

21. Tanaka M, Sakaguchi M, Yagita Y, et al. Thyroid antibodies are associated with stenotic lesions in the terminal portion of the internal carotid artery. Eur J Neurol. 2014; 21(6): 867-873.

22. Shi Z, Zhang X, Chen Z, et al. Elevated thyroid autoantibodies and intracranial stenosis in stroke at an early age. Int J Stroke. 2014; 9(6): 735-740.

23. Liu F, Feng J, Hao M, et al. Thyroid stimulating hormone correlates with triglyceride levels but is not associated with the severity of acute ischemic stroke in patients with euthyroidism: a cross-sectional study. Ann Transl Med. 2023; 11(2): 67.

24. Ramírez-Quiñones J, Wahlster S, Barrientos-Imán D, et al. Bilateral Ischemic Strokes Secondary to Moyamoya Syndrome Associated With Graves Thyrotoxicosis in a Patient of Amerindian Descent From Peru: A Case Report. Cureus. 2022; 14(7): e26546.

25. Huang GQ, Zeng YY, Cheng QQ, et al. Low triiodothyronine syndrome is associated with hemorrhagic transformation in patients with acute ischaemic stroke. Aging (Albany NY). 2019; 11(16): 6385-6397.

26. Nakamura K, Yanaka K, Ihara S, et al. Multiple intracranial arterial stenoses around the circle of Willis in association with Graves' disease: report of two cases. Neurosurgery. 2003; 53: 1210-1214.

27. Inaba M, Henmi Y, Kumeda Y, et al. Increased stiffness in common carotid artery in hyperthyroid Graves' disease patients. Biomed Pharmacother. 2002; 56: 241-246.

28. Yoshimoto T, Ishiyama H, Hattori Y, et al. Association of thyroid peroxidase antibody with the RNF213 p.R4810K variant in ischemic stroke/transient ischemic attack. doi: 10.1016/j.atherosclerosis.2023.117281. Epub 2023 Sep 12.